

AMENDMENTS TO THE CLAIMS

Claim 1 (Currently amended): A composition comprising chemically defined valency platform molecule comprising molecules, wherein the valency platform molecules individually comprise a high molecular weight polyethylene oxide group having a molecular weight of at least about 18,000 Daltons, and wherein said valency platform molecules have a polydispersity less than 1.2.

Claim 2 (Currently amended): The valency platform molecule composition of claim 1, wherein the valency platform molecules individually comprise a second comprising at least 2 high molecular weight polyethylene oxide groups group having a molecular weight of at least about 18,000 Daltons.

Claim 3 (Currently amended): The valency platform molecule composition of claim 1, wherein the high molecular weight polyethylene oxide group has a molecular weight of greater than about 22,000 Daltons.

Claim 4 (Currently amended): The valency platform molecule composition of claim 1, wherein the high molecular weight polyethylene oxide group has a molecular weight of at least greater than about 40,000 Daltons.

Claim 5 (Currently amended): The valency platform molecule composition of claim 1, wherein the high molecular weight polyethylene oxide group has the formula:



wherein n is greater than about 500.

Claim 6 (Currently amended): The ~~valency platform molecule composition~~ of claim 5, wherein n is greater than about 600.

Claim 7 (Currently amended): The ~~valency platform molecule composition~~ of claim 5, wherein n is greater than about 700.

Claim 8 (Currently amended): The ~~valency platform molecule composition~~ of claim 5, wherein n is greater than about 800.

Claim 9 (Currently amended): The ~~valency platform molecule composition~~ of claim 1, wherein the valency platform molecule ~~comprises~~ molecules individually comprise ~~comprises~~ a core group and at least three arms wherein each arm comprises a terminus.

Claim 10 (Currently amended): The ~~valency platform molecule composition~~ of claim 9, wherein the core group comprises [[a]] the high molecular weight polyethylene oxide group.

Claim 11 (Currently amended): The ~~valency platform molecule composition~~ of claim 9, wherein ~~at least one of said arms~~ an arm comprises [[a]] the high molecular weight polyethylene oxide group.

Claim 12 (Currently amended): The ~~valency platform molecule composition~~ of claim 9, wherein the high molecular weight polyethylene oxide group is attached to the core or ~~arm~~ one of said arms.

Claim 13 (Canceled)

Claim 14 (Currently amended): The valency platform molecule composition of claim 1, wherein the valency platform molecules individually comprise comprising at least three reactive conjugating groups selected from the group consisting of hydroxyl, thiol, isocyanate, isothiocyanate, amine, alkyl halide, alkylmercurial halide, aldehyde, ketone, carboxylic acid halide, α -halocarbonyl, α,β -unsaturated carbonyl, haloformate ester, carboxylic acid, carboxylic ester, carboxylic anhydride, O-acyl isourea, hydrazide, maleimide, imidate ester, sulfonate ester, sulfonyl halide, α,β -unsaturated sulfone, aminoxy, semicarbazide, and β -aminothiol.

Claim 15 (Currently amended): The valency platform molecule composition of claim 1, wherein the valency platform molecules individually comprise comprising at least 3 aminoxy groups.

Claim 16 (Currently amended): The valency platform molecule composition of claim 1, wherein the valency platform molecules individually comprise comprising at least 3 carbamate groups.

Claim 17 (Currently amended): ~~A conjugate of a valency platform molecule of claim 1 and a biologically active molecule. A composition comprising conjugates comprising biologically active molecules and the valency platform molecules according to claim 1.~~

Claim 18 (Currently amended): The conjugate composition of claim 17, wherein the biologically active molecule is molecules are selected from the group consisting of a polysaccharide, a polypeptide, a nucleic acid, and a lipid polysaccharides, polypeptides, nucleic acids, and lipids.

Claim 19 (Currently amended): The conjugate composition of claim 17, wherein the conjugate is a B cell toleragen conjugates are B cell toleragens.

Claim 20 (Currently amended): The conjugate composition of claim 18, wherein the biologically active molecule comprises molecules comprise a nucleic acid or analog thereof, which specifically binds to an anti-double stranded DNA antibody.

Claim 21 (Currently amended): The conjugate composition of claim 19, wherein the biologically active molecule is a molecules are β_2 GPI domain 1 polypeptide polypeptides or analog analogs thereof that specifically binds bind to a β_2 GPI-dependent antiphospholipid antibody.

Claim 22 (Currently amended): The conjugate composition of claim 21, wherein the conjugate is conjugates are effective for the treatment of antibody mediated thrombosis.

Claim 23 (Currently amended): The conjugate composition of claim 18, wherein the biologically active molecule is an molecules are α Gal epitope epitopes or analog analogs thereof that specifically binds bind to an anti- α Gal antibody.

Claim 24 (Currently amended): A pharmaceutically acceptable composition comprising the conjugate composition of claim 17 and a pharmaceutically acceptable carrier.

Claim 25 (Currently amended): A conjugate [[of]] comprising a chemically defined valency platform molecule and a polypeptide comprising a β_2 GPI domain 1 polypeptide, wherein the conjugate comprises a high molecular weight polyethylene oxide group having a molecular weight of at least about 18,000 Daltons.

Claim 26 (original): The conjugate of claim 25, wherein the valency platform molecule comprises at least 3 aminoxy groups.

Claim 27 (original): The conjugate of claim 25, wherein the valency platform molecule comprises at least 3 carbamate groups.

Claim 28 (previously presented): The conjugate of claim 25, wherein the high molecular weight polyethylene oxide group has a molecular weight greater than about 22,000 Daltons.

Claim 29 (original): The conjugate of claim 25, wherein the valency platform molecule comprises a core group and at least three arms, wherein each arm comprises a terminus.

Claim 30 (original): The conjugate of claim 25, wherein the polypeptide specifically binds to a β_2 GPI-dependent antiphospholipid antibody.

Claim 31 (original): The conjugate of claim 30, wherein the polypeptide lacks a T cell epitope capable of activating T cells in an individual having β_2 GPI dependent antiphospholipid antibodies.

Claim 32 (original): The conjugate of claim 25, wherein the β_2 GPI domain 1 polypeptide comprises at least five contiguous amino acids of Figure 19 (SEQ ID NO: 2).

Claim 33 (original): The conjugate of claim 25, wherein the β_2 GPI domain 1 polypeptide comprises amino acids Nos. 2-63 of SEQ ID NO: 2.

Claim 34 (previously presented): The conjugate of claim 25, wherein the conjugate is selected from the group consisting of compounds 200, 202, 203, and 205 shown in Figure 7 and compound 300 shown in Figure 16, wherein D1 in said structures is a polypeptide consisting of amino acids No. 2-63 of SEQ ID NO: 2.

Claim 35 (Currently amended): The conjugate composition of claim 23, wherein the biologically active molecule is an molecules are said α Gal epitope epitopes.

Claim 36 (previously presented): The conjugate of claim 25, wherein the conjugate is effective for the treatment of antibody mediated thrombosis.

Claim 37 (Currently amended): The conjugate composition of claim 17, wherein the average total molecular weight of the conjugate conjugates is no greater than about 200,000 Daltons.

Claim 38 (Currently amended): The conjugate composition of claim 17, wherein the high molecular weight polyethylene oxide group has a molecular weight of greater than about 22,000 Daltons.

Claim 39 (Currently amended): The conjugate composition of claim [[17]] 1, wherein the high molecular weight polyethylene oxide group has a molecular weight of greater than about 30,000 Daltons.

Claim 40 (Currently amended): The conjugate composition of claim 17, wherein the high molecular weight polyethylene oxide group has a molecular weight of greater than about 40,000 Daltons.

Claim 41 (Currently amended): The conjugate composition of claim [[17]] 1, wherein the high molecular weight polyethylene oxide group has a molecular weight of greater than about 50,000 Daltons.

Claim 42 (Currently amended): The conjugate composition of claim [[17]] 1, wherein the high molecular weight polyethylene oxide group has a molecular weight of greater than about 100,000 Daltons.

Claim 43 (Currently amended): The conjugate composition of claim 17, wherein the high molecular weight polyethylene oxide group has the formula:



wherein n is greater than about 500.

Claim 44 (Currently amended): The conjugate composition of claim 43, wherein n is greater than about 600.

Claim 45 (Currently amended): The ~~conjugate~~ composition of claim 43, wherein n is greater than about 700.

Claim 46 (Currently amended): The ~~conjugate~~ composition of claim 43, wherein n is greater than about 800.

Claim 47 (Currently amended): The ~~conjugate~~ composition of claim [[43]] 5, wherein n is greater than about 900.

Claim 48 (Currently amended): The ~~conjugate~~ composition of claim [[43]] 5, wherein n is about 400 to 550.

Claim 49 (Currently amended): The ~~conjugate~~ composition of claim [[43]] 5, wherein n is 520 to 600.

Claim 50 (Currently amended): The ~~conjugate~~ composition of claim [[43]] 5, wherein n is 600 to 800.

Claim 51 (Currently amended): The ~~conjugate~~ composition of claim [[43]] 5, wherein n is 600 to 1000.

Claim 52 (Currently amended): The ~~conjugate~~ composition of claim 17, wherein the valency platform ~~molecule~~ comprises molecules individually comprise a second high molecular weight polyethylene oxide group having a molecular weight of at least about 18,000 Da.

Claim 53 (Currently amended): The ~~conjugate~~ composition of claim 17, wherein the valency platform ~~molecule~~ comprises molecules individually comprise a core group and at least three arms wherein each arm comprises a terminus.

Claim 54 (Currently amended): The ~~conjugate~~ composition of claim 53, wherein the core group comprises the high molecular weight polyethylene oxide group.

Claim 55 (Currently amended): The ~~conjugate composition~~ of claim 53, wherein ~~one of said arms~~ ~~an arm~~ comprises the high molecular weight polyethylene oxide group.

Claim 56 (Currently amended): The ~~conjugate composition~~ of claim 53, wherein the high molecular weight polyethylene oxide group is attached to the core or one of said arms.

Claim 57 (Canceled)

Claim 58 (Currently amended): The ~~conjugate composition~~ of claim 17, wherein the valency platform ~~molecule comprises molecules~~ ~~individually comprise~~ at least three reactive conjugating groups selected from the group consisting of hydroxyl, thiol, isocyanate, isothiocyanate, amine, alkyl halide, alkylmercurial halide, aldehyde, ketone, carboxylic acid halide, α -halocarbonyl, α, β -unsaturated carbonyl, haloformate ester, carboxylic acid, carboxylic ester, carboxylic anhydride, O-acyl isourea, hydrazide, maleimide, imidate ester, sulfonate ester, sulfonyl halide, α, β -unsaturated sulfone, aminoxy, semicarbazide, and β -aminothiol.

Claim 59 (Currently amended): The ~~conjugate composition~~ of claim 17, wherein the valency platform ~~molecule comprises molecules~~ ~~individually comprise~~ at least 3 aminoxy groups.

Claim 60 (Currently amended): The ~~conjugate composition~~ of claim 17, wherein the valency platform ~~molecule comprises molecules~~ ~~individually comprise~~ at least 3 carbamate groups.

Claim 61 (Currently amended): A ~~conjugate of a composition comprising~~ chemically defined valency platform ~~molecule and a biologically active molecule~~ ~~molecules~~, wherein the chemically defined valency platform ~~molecule comprises molecules~~ ~~individually comprise~~ a first and a second polyethylene oxide group, ~~each having~~ ~~wherein the first and the second polyethylene oxide groups each have~~ a molecular weight of greater than about 5,000 Da, and wherein the total of the molecular weights of all polyethylene oxide groups in ~~the~~ ~~each~~ valency platform molecule in combination is greater than about 18,000 Da, ~~and wherein said valency platform molecules have a polydispersity less than 1.2.~~

Claim 62 (Currently amended): The ~~conjugate~~ composition of claim 61, wherein the molecular weight of all polyethylene oxide groups in ~~the~~ each valency platform molecule in combination is greater than about 20,000 Da.

Claim 63 (Currently amended): The ~~conjugate~~ composition of claim 61, wherein the molecular weight of all polyethylene oxide groups in ~~the~~ each valency platform molecule in combination is greater than about 22,000 Da.

Claim 64 (Currently amended): The ~~conjugate~~ composition of claim 61, wherein the molecular weight of all polyethylene oxide groups in ~~the~~ each valency platform molecule in combination is greater than about 30,000 Da.

Claim 65 (Currently amended): The ~~conjugate~~ composition of claim 61, wherein the molecular weight of all polyethylene oxide groups in ~~the~~ each valency platform molecule in combination is greater than about 40,000 Da.

Claim 66 (Currently amended): The ~~conjugate~~ composition of claim 61, wherein the molecular weight of all polyethylene oxide groups in ~~the~~ each valency platform molecule in combination is greater than about 35,200 Da.

Claim 67 (Currently amended): The ~~conjugate~~ composition of claim 61, wherein the molecular weight of all polyethylene oxide groups in ~~the~~ each valency platform molecule in combination is greater than about 39,600 Da.

Claim 68 (Currently amended): The ~~conjugate~~ composition of claim 61, wherein the molecular weight of all polyethylene oxide groups in ~~the~~ each valency platform molecule in combination is greater than about 44,000 Da.

Claim 69 (Currently amended): The ~~conjugate~~ composition of claim 61, wherein the molecular weight of all polyethylene oxide groups in ~~the~~ each valency platform molecule in combination is 22,900-26,400 Da.

Claim 70 (Currently amended): The ~~conjugate composition~~ of claim 61, wherein the molecular weight of all polyethylene oxide groups in ~~the~~ each valency platform molecule in combination is 24,200-30,800 Da.

Claim 71 (Currently amended): The ~~conjugate composition~~ of claim 61, wherein the molecular weight of all polyethylene oxide groups in ~~the~~ each valency platform molecule in combination is 26,400-44,000 Da.

Claim 72 (Currently amended): The ~~conjugate composition~~ of claim 61, wherein the molecular weight of all polyethylene oxide groups in ~~the~~ each valency platform molecule in combination is 26,400-39,600 Da.

Claim 73 (Currently amended): The ~~conjugate composition~~ of claim 61, wherein the molecular weight of all polyethylene oxide groups in ~~the~~ each valency platform molecule in combination is 26,400-35,200 Da.

Claim 74 (Currently amended): The ~~conjugate composition~~ of claim 61, wherein the first and the second polyethylene oxide groups each have a molecular weight of greater than about 10,000 Da.

Claim 75 (Currently amended): The ~~conjugate composition~~ of claim 61, wherein the first and the second polyethylene oxide groups each have a molecular weight of about 5,000-10,000 Da.

Claim 76 (Currently amended): The ~~conjugate composition~~ of claim 61, wherein the first and the second polyethylene oxide groups each have a molecular weight of about 8,000-20,000 Da.

Claim 77 (Currently amended): The ~~conjugate composition~~ of claim 61, wherein the first and the second polyethylene oxide groups each have a molecular weight of about 10,000-20,000 Da.

Claim 78 (Currently amended): The ~~conjugate composition~~ of claim 61, wherein the chemically defined valency platform molecule ~~comprises molecules individually comprise~~ a third and a fourth polyethylene oxide group.

Claim 79 (Currently amended): The ~~conjugate composition~~ of claim 78, wherein the first, second, third, and fourth polyethylene oxide groups each have a molecular weight of about 8,000-20,000 Da.

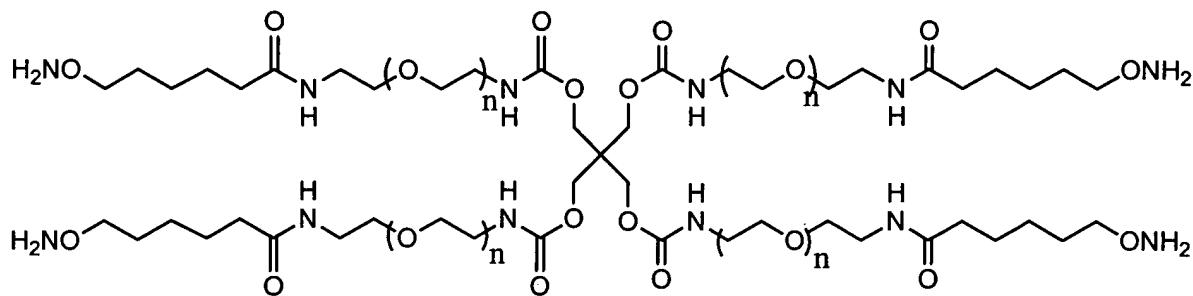
Claim 80 (Currently amended): The ~~conjugate composition~~ of claim 78, wherein the molecular weight of the first, second, third, and fourth polyethylene oxide groups ~~in each valency platform molecule~~ in combination is 26,400-44,000 Da.

Claim 81 (Currently amended): The ~~conjugate composition~~ of claim 61 ~~96~~, wherein the biologically active ~~molecule is a~~ ~~molecules are~~ β_2 GPI domain I polypeptide polypeptides or analog analogs thereof that specifically binds to a β_2 GPI-dependent antiphospholipid antibody.

Claim 82 (Currently amended): The ~~conjugate composition~~ of claim 81, wherein the biologically active ~~molecule is a~~ ~~molecules are~~ β_2 GPI domain I polypeptide polypeptides.

Claim 83 (Currently amended): ~~The conjugate of claim 80, wherein the biologically active molecule is a β_2 GPI domain I polypeptide. A composition comprising conjugates comprising biologically active molecules and the valency platform molecules of claim 80, wherein the biologically active molecules are β_2 GPI domain I polypeptides.~~

Claim 84 (Currently amended): ~~The conjugate of claim 61, wherein the conjugate has A chemically defined valency platform molecule having the formula:~~



or an aminoxy protected form thereof; wherein the molecular weight of the ~~first, second, third, and fourth~~ polyethylene oxide groups in combination is 26,400-44,000 Da.

Claim 85 (Currently amended): A conjugate of a chemically defined valency platform molecule and a biologically active molecule, wherein the valency platform molecule prior to conjugation with the biologically active molecule has having the formula:



or an aminoxy protected form thereof;

wherein y is 2 to 16;

n is 1 to 32;

R_c is H;

R_c is a hydrocarbyl group having from 1 to 200 carbon atoms;

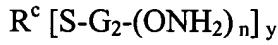
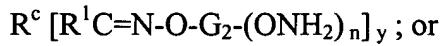
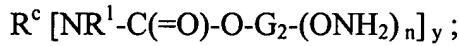
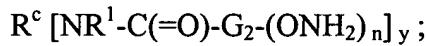
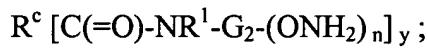
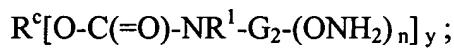
each G_2 independently comprises a polyethylene oxide group having a molecular weight of 44 to 22,000 Da;

wherein each G_2 further comprises an amide group;

with the proviso that the formula comprises at least a first and a second G₂ group, wherein the molecular weight of the polyethylene oxide groups in the first and the second G₂ groups are greater than about 5,000 Da; and

wherein the total of the molecular weights of all polyethylene oxide groups in the valency platform molecule in combination is greater than about 18,000 Da.

Claim 86 (Currently amended): A ~~conjugate of a chemically defined valency platform molecule and a biologically active molecule, wherein the valency platform molecule prior to conjugation with the biologically active molecule has~~ having the structure of one of the following formulae:



or an aminoxy protected form thereof;

wherein:

y is 1 to 16;

n is 1 to 32;

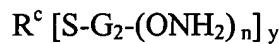
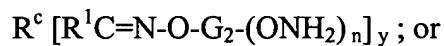
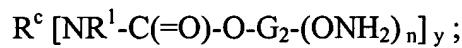
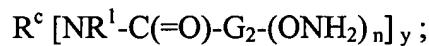
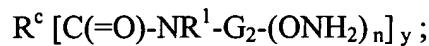
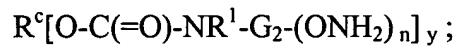
R¹ is H, alkyl, heteroalkyl, aryl, heteroaryl or G₂-(ONH₂)_n;

R^c is an organic moiety comprising atoms selected from the group consisting of H, C, N, O, P, Si and S atoms, and optionally comprising one or more polyethylene oxide groups; and

G_2 is an organic moiety comprising atoms selected from the group consisting of H, C, N, O, P, Si and S atoms, and optionally comprising one or more polyethylene oxide groups;

with the proviso that at least one of the R^c or G_2 groups comprises a high molecular weight polyethylene oxide group having a molecular weight of at least greater than about 18,000 Da.

Claim 87 (Currently amended): A ~~conjugate of a chemically defined valency platform molecule and a biologically active molecule, wherein the valency platform molecule prior to conjugation with the biologically active molecule has~~ having the structure of one of the following formulae:



or an aminoxy protected form thereof;

wherein:

y is 1 to 16;

n is 1 to 32;

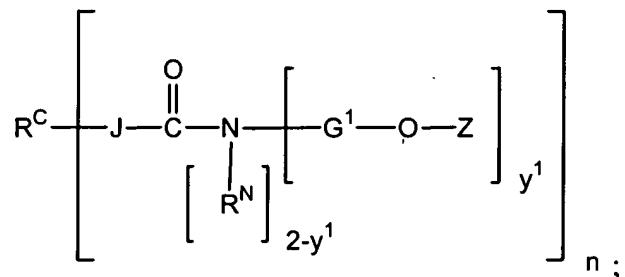
R¹ is H, alkyl, heteroalkyl, aryl, heteroaryl or G₂-(ONH₂)_n;

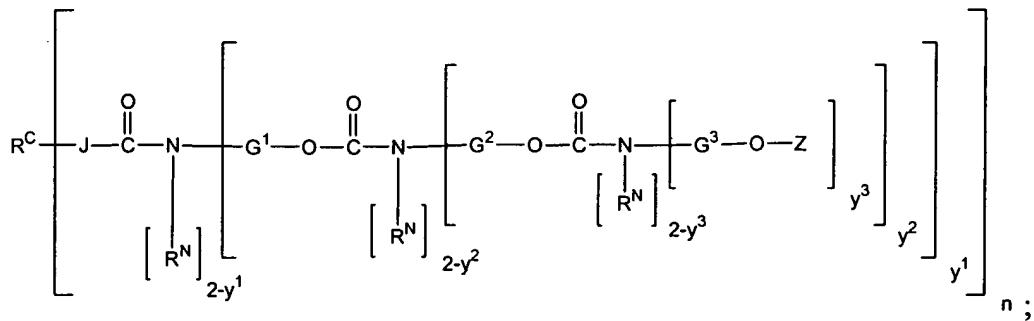
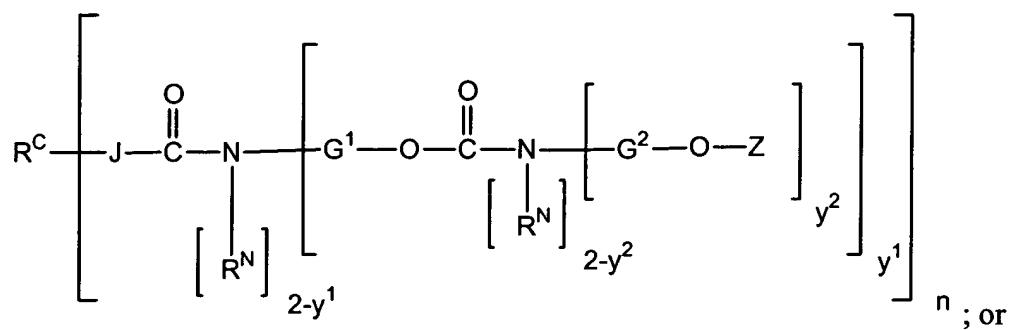
R^c is an organic moiety comprising atoms selected from the group consisting of H, C, N, O, P, Si and S atoms, and optionally comprising one or more polyethylene oxide groups; and

G₂ is an organic moiety comprising atoms selected from the group consisting of H, C, N, O, P, Si and S atoms, and optionally comprising one or more polyethylene oxide groups;

with the proviso that the valency platform molecule comprises at least 2 polyethylene oxide groups each having a molecular weight of greater than about 5,000 Da, and wherein the total of the molecular weights of all polyethylene oxide groups in the valency platform molecule in combination is greater than about 18,000 Da.

Claim 88 (Currently amended): A ~~conjugate of a chemically defined valency platform molecule and a biologically active molecule, wherein the valency platform molecule prior to conjugation with the biologically active molecule has~~ having the structure of one of the following formulae:





wherein:

n is an integer from 1 to 10;

y^1 , y^2 , and y^3 are independently 1 or 2;

J independently denotes either an oxygen atom or a covalent bond;

R^c is selected from the group consisting of:

hydrocarbyl groups having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, and hydrogen atoms, and having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, nitrogen, and hydrogen atoms, and having from 1 to 20 carbon atoms; and

organic groups consisting only of carbon, oxygen, sulfur, and hydrogen atoms, and having from 1 to 20 carbon atoms;

and wherein R^c optionally further comprises one or more polyethylene oxide groups;

each G^1 , G^2 , and G^3 is independently selected from the group consisting of:

hydrocarbyl groups having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, and hydrogen atoms, and having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, nitrogen, and hydrogen atoms, and having from 1 to 20 carbon atoms;

and wherein each G^1 , G^2 , and G^3 may independently further comprise one or more polyethylene oxide groups;

each R^N is independently selected from the group consisting of:

hydrogen;

linear or branched alkyl groups having from 1 to 15 carbon atoms;

alkyl groups comprising an alicyclic structure and having from 1 to 15 carbon atoms;

aromatic groups having from 6 to 20 carbon atoms;

heteroaromatic groups having from 3 to 20 carbon atoms;

each Z is independently selected from the group consisting of:

-H

-C(=O)OR^{CARB}

-C(=O)R^{ESTER}

-C(=O)NR^AR^B

-C(=O)NR^{AB}

wherein:

each R^{CARB} is independently an organic group comprising from 1 to about 20 carbon atoms;

each R^{ESTER} is independently an organic group comprising from 1 to about 20 carbon atoms;

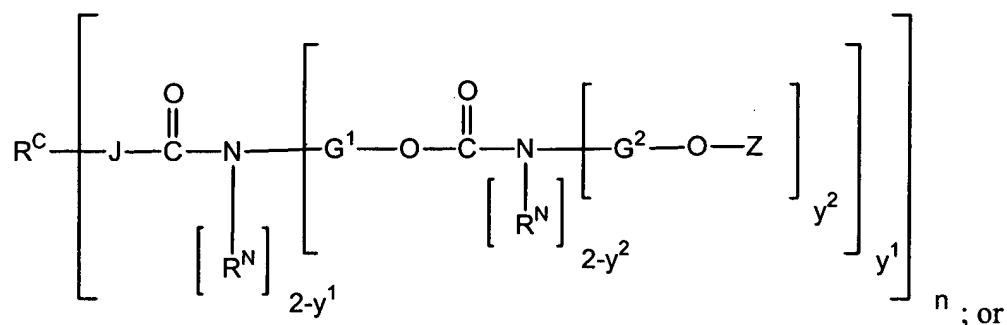
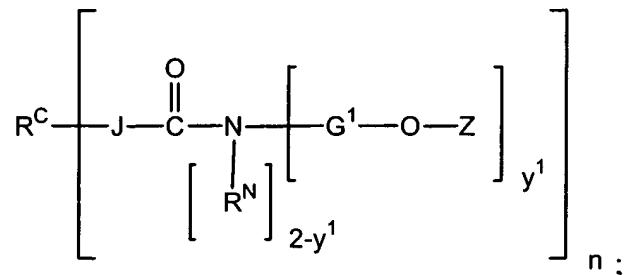
each monovalent R^A and R^B and each divalent R^{AB} is independently H or an organic group comprising from 1 to 20 carbon atoms, and further comprising a reactive conjugating functional group;

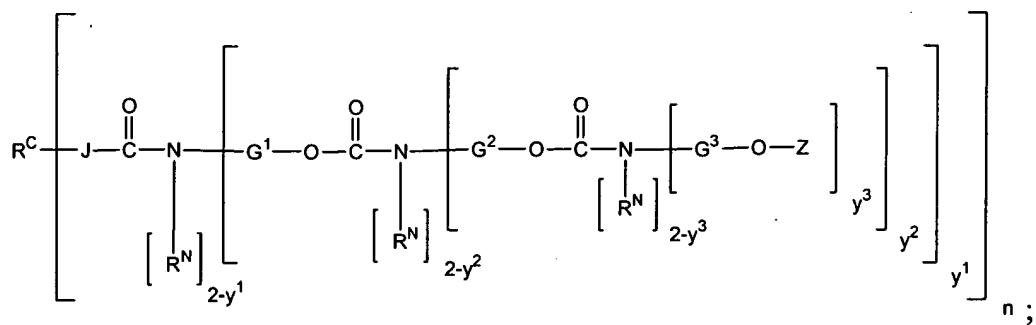
~~each divalent R^{AB} is independently an organic group comprising from 1 to 20 carbon atoms; and~~

~~wherein, when Z is -C(=O)OR^{CARB}, -C(=O)R^{ESTER}, -C(=O)NR^AR^B, or -C(=O)NR^{AB}, Z further comprises a reactive conjugating functional group;~~

with the proviso that at least one of the R^c , G^1 , G^2 , or G^3 groups comprises a high molecular weight polyethylene oxide group having a molecular weight of at least greater than about 18,000 Da.

Claim 89 (Currently amended): A ~~conjugate of a chemically defined valency platform molecule and a biologically active molecule, wherein the valency platform molecule prior to conjugation with the biologically active molecule has~~ having the structure of one of the following formulae:





wherein:

n is an integer from 1 to 10;

y^1 , y^2 , and y^3 are independently 1 or 2;

J independently denotes either an oxygen atom or a covalent bond;

R^c is selected from the group consisting of:

hydrocarbyl groups having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, and hydrogen atoms, and having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, nitrogen, and hydrogen atoms, and having from 1 to 20 carbon atoms; and

organic groups consisting only of carbon, oxygen, sulfur, and hydrogen atoms, and having from 1 to 20 carbon atoms;

and wherein R^c optionally further comprises one or more polyethylene oxide groups;

each G^1 , G^2 , and G^3 is independently selected from the group consisting of:

hydrocarbyl groups having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, and hydrogen atoms, and having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, nitrogen, and hydrogen atoms, and having from 1 to 20 carbon atoms;

and wherein each G¹, G², and G³ may independently further comprise one or more polyethylene oxide groups;

each R^N is independently selected from the group consisting of:

hydrogen;

linear or branched alkyl groups having from 1 to 15 carbon atoms;

alkyl groups comprising an alicyclic structure and having from 1 to 15 carbon atoms;

aromatic groups having from 6 to 20 carbon atoms;

heteroaromatic groups having from 3 to 20 carbon atoms;

each Z is independently selected from the group consisting of:

-H

-C(=O)OR^{CARB}

-C(=O)R^{ESTER}

-C(=O)NR^AR^B

$-\text{C}(=\text{O})\text{NR}^{\text{AB}}$

wherein:

each R^{CARB} is independently an organic group comprising from 1 to about 20 carbon atoms;

each R^{ESTER} is independently an organic group comprising from 1 to about 20 carbon atoms;

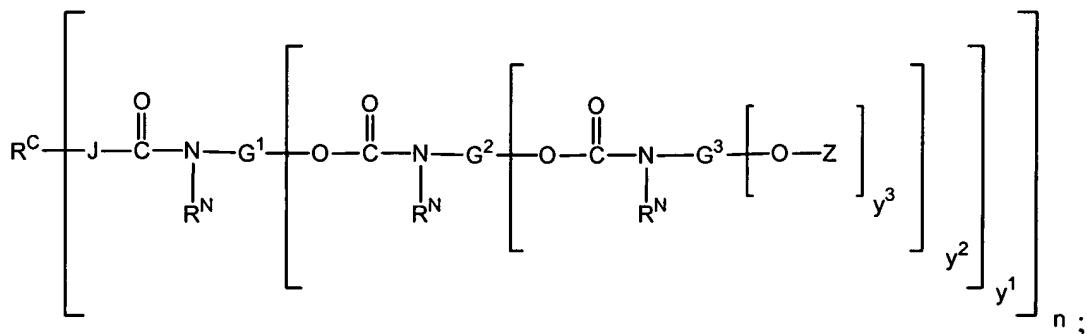
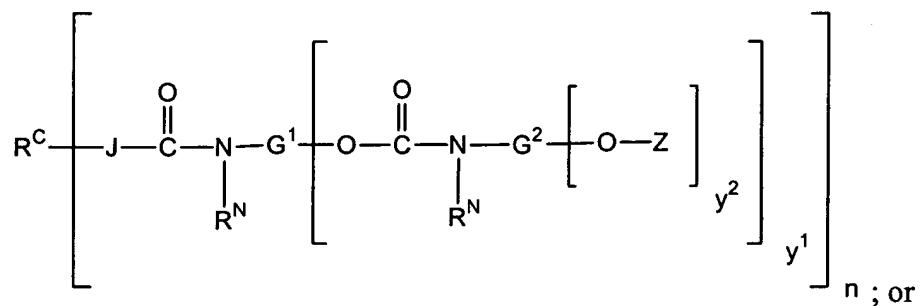
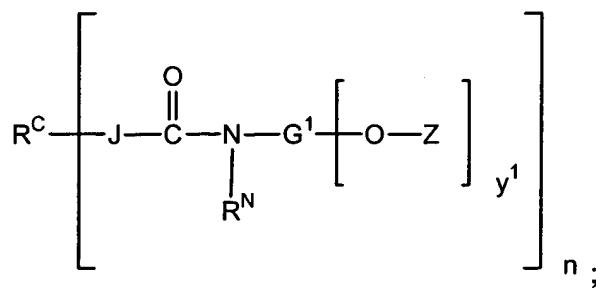
each monovalent R^{A} and R^{B} and each divalent R^{AB} is independently H or an organic group comprising from 1 to 20 carbon atoms, and further comprising a reactive conjugating functional group;

each divalent R^{AB} is independently an organic group comprising from 1 to 20 carbon atoms; and

wherein, when Z is $\text{C}(-\text{O})\text{OR}^{\text{CARB}}$, $\text{C}(-\text{O})\text{R}^{\text{ESTER}}$, $\text{C}(-\text{O})\text{NR}^{\text{A}}\text{R}^{\text{B}}$, or $\text{C}(-\text{O})\text{NR}^{\text{AB}}$, Z further comprises a reactive conjugating functional group;

with the proviso that the valency platform molecule comprises at least 2 polyethylene oxide groups each having a molecular weight of greater than about 5,000 Da, and wherein the total of the molecular weights of all polyethylene oxide groups in the valency platform molecule in combination is greater than about 18,000 Da.

Claim 90 (Currently amended): A conjugate of a chemically defined valency platform molecule and a biologically active molecule, wherein the valency platform molecule prior to conjugation with the biologically active molecule has having the structure of one of the following formulae:



wherein:

n is an integer from 1 to 10;

y^1 , y^2 , and y^3 are independently a positive integer from 1 to 10;

J independently denotes either an oxygen atom or a covalent bond;

R^C is selected from the group consisting of:

hydrocarbyl groups having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, and hydrogen atoms, and having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, nitrogen, and hydrogen atoms, and having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, sulfur, and hydrogen atoms, and having from 1 to 20 carbon atoms;

and wherein R^c optionally further comprises one or more polyethylene oxide group;

each G^1 , G^2 , and G^3 is independently selected from the group consisting of:

hydrocarbyl groups having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, and hydrogen atoms, and having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, nitrogen, and hydrogen atoms, and having from 1 to 20 carbon atoms;

and wherein each G^1 , G^2 , and G^3 may independently further comprise one or more polyethylene oxide groups;

each R^N is independently selected from the group consisting of:

hydrogen;

linear or branched alkyl groups having from 1 to 15 carbon atoms;

alkyl groups comprising an alicyclic structure and having from 1 to 15 carbon atoms;

aromatic groups having from 6 to 20 carbon atoms;

heteroaromatic groups having from 3 to 20 carbon atoms;

each Z is independently selected from the group consisting of:

-H

-C(=O)OR^{CARB}

-C(=O)R^{ESTER}

-C(=O)NR^AR^B

-C(=O)NR^{AB}

wherein:

each R^{CARB} is independently an organic group comprising from 1 to about 20 carbon atoms;

each R^{ESTER} is independently an organic group comprising from 1 to about 20 carbon atoms;

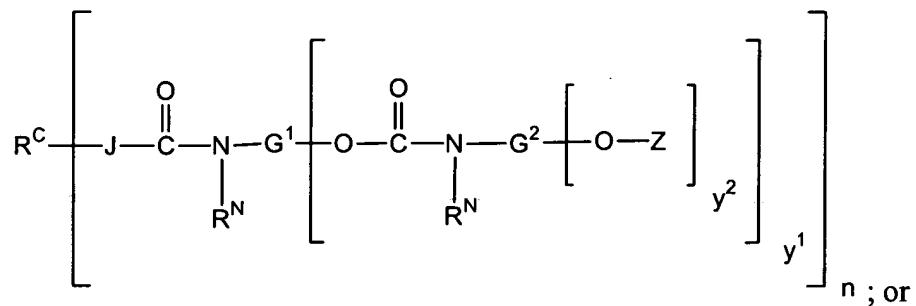
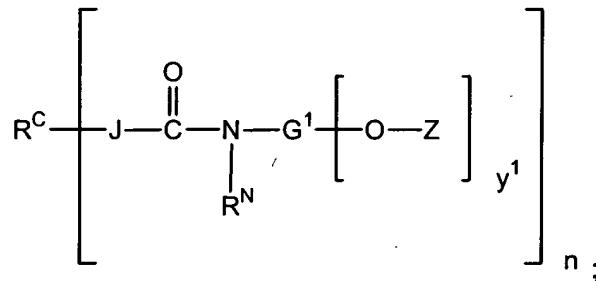
each monovalent R^A and R^B and each divalent R^{AB} is independently H or an organic group comprising from 1 to 20 carbon atoms, and further comprising a reactive conjugating functional group;

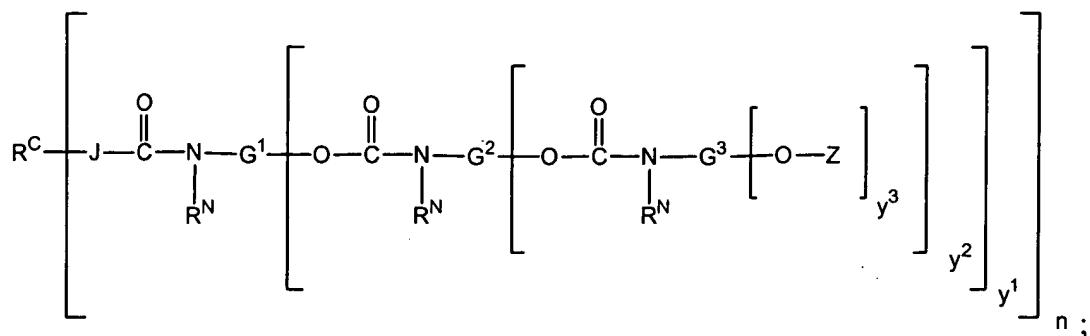
each divalent R^{AB} is independently an organic group comprising from 1 to 20 carbon atoms; and

wherein, when Z is $\text{C}(\text{=O})\text{OR}^{\text{CARB}}$, $\text{C}(\text{=O})\text{R}^{\text{ESTER}}$, $\text{C}(\text{=O})\text{NR}^{\text{A}}\text{R}^{\text{B}}$, or $\text{C}(\text{=O})\text{NR}^{\text{AB}}$, Z further comprises a reactive conjugating functional group;

with the proviso that at least one of the R^{C} , G^1 , G^2 , or G^3 groups comprises a high molecular weight polyethylene oxide group having a molecular weight of at least greater than about 18,000 Da.

Claim 91 (Currently amended): A conjugate of a chemically defined valency platform molecule and a biologically active molecule, wherein the valency platform molecule prior to conjugation with the biologically active molecule has having the structure of one of the following formulae:





wherein:

n is an integer from 1 to 10;

y^1 , y^2 , and y^3 are independently a positive integer from 1 to 10;

J independently denotes either an oxygen atom or a covalent bond;

R^C is selected from the group consisting of:

hydrocarbyl groups having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, and hydrogen atoms, and having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, nitrogen, and hydrogen atoms, and having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, sulfur, and hydrogen atoms, and having from 1 to 20 carbon atoms;

and wherein R^C optionally further comprises one or more polyethylene oxide groups;

each G^1 , G^2 , and G^3 is independently selected from the group consisting of:

hydrocarbyl groups having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, and hydrogen atoms, and having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, nitrogen, and hydrogen atoms, and having from 1 to 20 carbon atoms;

and wherein each G¹, G², and G³ may independently further comprise one or more polyethylene oxide groups;

each R^N is independently selected from the group consisting of:

hydrogen;

linear or branched alkyl groups having from 1 to 15 carbon atoms;

alkyl groups comprising an alicyclic structure and having from 1 to 15 carbon atoms;

aromatic groups having from 6 to 20 carbon atoms;

heteroaromatic groups having from 3 to 20 carbon atoms;

each Z is independently selected from the group consisting of:

-H

-C(=O)OR^{CARB}

-C(=O)R^{ESTER}

-C(=O)NR^AR^B

$-C(=O)NR^{AB}$

wherein:

each R^{CARB} is independently an organic group comprising from 1 to about 20 carbon atoms;

each R^{ESTER} is independently an organic group comprising from 1 to about 20 carbon atoms;

each monovalent R^A and R^B and each divalent R^{AB} is independently H or an organic group comprising from 1 to 20 carbon atoms, and further comprising a reactive conjugating functional group;

~~each divalent R^{AB} is independently an organic group comprising from 1 to 20 carbon atoms; and~~

~~wherein, when Z is $C(=O)OR^{CARB}$, $C(=O)R^{ESTER}$, $C(=O)NR^A R^B$, or $-C(=O)NR^{AB}$, Z further comprises a reactive conjugating functional group;~~

with the proviso that the valency platform molecule comprises at least 2 polyethylene oxide groups each having a molecular weight of greater than about 5,000 Da, and wherein the total of the molecular weights of all polyethylene oxide groups in the valency platform molecule in combination is greater than about 18,000 Da.

Claim 92 (Currently amended): A ~~conjugate of a~~ chemically defined valency platform molecule ~~and a biologically active molecule, wherein the valency platform molecule prior to conjugation with the biologically active molecule has~~ having the structure of one of the following formulae:

$$G^{[1]} \quad \left\{ \quad T^{[1]} \quad \right\} \quad n^{[1]} ; \text{ or}$$

$$G^{[2]} \quad \left\{ \quad L^{[2]} - J^{[2]} - Z^{[2]} (T^{[2]})_{p[2]} \quad \right\} \quad n^{[2]} ;$$

wherein

each of $G^{[1]}$ and $G^{[2]}$, if present, is independently a linear, branched or multiply-branched chain comprising 1-2,000 chain atoms selected from the group C, N, O, Si, P and S;

and wherein $G^{[1]}$ and $G^{[2]}$, if present, optionally further comprises one or more polyethylene oxide groups;

each $T^{[1]}$ and each $T^{[2]}$, if present, is independently chosen from the group NHR^{SUB} , $C(=O)NHNHR^{SUB}$, $NHNHR^{SUB}$, $C(=O)OH$, $C(=O)OR^{ESTER}$, $C(=O)OC(=O)R^B$, $C(=O)X$, $S(=O)_2X$, $C(=NR^{SUB})OR^{SUB}$, NCO , NCS , $OC(=O)X$, $C(=O)OC(=NR^{SUB})NHR^{SUB}$, $C(=O)H$, $C(=O)R^B$, SH , OH , $C(=O)CH_2X$, $R^{ALK}X$, $S(=O)_2OR^{ALK}X$, $N-C(=O)CH=CHC(=O)-NR^1R^2$ wherein R^1R^2 is $-C(=O)CH=CHC(=O)-$, $C(=O)CR^B=CR^B_2$, $R^{ALK}-Hg-X$, $S(=O)CR^B=CR^B_2$, and ONH_2 ;

wherein

each X is independently a halogen of atomic number greater than 16 and less than 54 or other leaving group;

each R^{ALK} is independently a linear, branched, or cyclic alkyl (1-20C) group;

each R^{SUB} is independently H, linear, branched, or cyclic alkyl (1-20C), aryl (6-20C), or alkaryl (7-30C);

each R^{ESTER} is independently N-succinimidyl, p-nitrophenyl, pentafluorophenyl, tetrafluorophenyl, pentachlorophenyl, 2,4,5-trichlorophenyl, 2,4-dinitrophenyl, cyanomethyl, 5-chloro,8-quinolone, 1-piperidine, or N-benzotriazole;

each R^B is independently a radical comprising 1-50 atoms selected from the group C, H, N, O, Si, P and S;

each $L^{[2]}$, if present, is independently chosen from the group O, NR^{SUB} and S;

each $J^{[2]}$, if present, is independently chosen from the group C(=O) and C(=S);

each $Z^{[2]}$, if present, is independently a radical comprising 1-200 atoms selected from the group C, H, N, O, Si, P and S, and forming attachment sites for at least $p^{[2]}$ functional groups, wherein the attachment sites are alkyl, alkenyl, or aromatic carbon atoms;

and wherein $Z^{[2]}$, if present, optionally further comprises one or more polyethylene oxide groups;

$n^{[1]}$, if present, is 1 to 32;

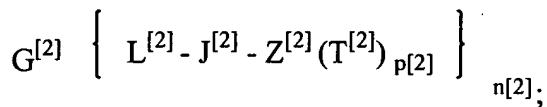
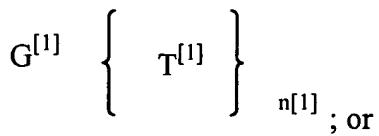
$n^{[2]}$, if present, is 1 to 32; and

$p^{[2]}$, if present, is 1 to 8; with the proviso that the product $n^{[2]} \times p^{[2]}$ be greater than 1 and less than 33;

with the proviso that at least one of the $G^{[1]}$, $G^{[2]}$, or $Z^{[2]}$ groups comprises a high molecular weight polyethylene oxide group having a molecular weight of at least greater than about 18,000 Da.

Claim 93 (Currently amended): A ~~conjugate of a chemically defined valency platform molecule and a biologically active molecule, wherein the valency platform molecule prior to~~

~~conjugation with the biologically active molecule has~~ having the structure of one of the following formulae:



wherein

each of $G^{[1]}$ and $G^{[2]}$, if present, is independently a linear, branched or multiply-branched chain comprising 1-2,000 chain atoms selected from the group C, N, O, Si, P and S;

and wherein $G^{[1]}$ and $G^{[2]}$, if present, optionally further comprises one or more polyethylene oxide groups;

each $T^{[1]}$ and each $T^{[2]}$, if present, is independently chosen from the group NHR^{SUB} , $C(=O)NHNHR^{SUB}$, $NHNHR^{SUB}$, $C(=O)OH$, $C(=O)OR^{ESTER}$, $C(=O)OC(=O)R^B$, $C(=O)X$, $S(=O)_2X$, $C(=NR^{SUB})OR^{SUB}$, NCO , NCS , $OC(=O)X$, $C(=O)OC(=NR^{SUB})NHR^{SUB}$, $C(=O)H$, $C(=O)R^B$, SH , OH , $C(=O)CH_2X$, $R^{ALK}X$, $S(=O)_2OR^{ALK}X$, $N-C(=O)CH=CHC(=O)-NR^1R^2$ wherein R^1R^2 is $-C(=O)CH=CHC(=O)-$, $C(=O)CR^B=CR^B_2$, $R^{ALK}-Hg-X$, $S(=O)CR^B=CR^B_2$, and ONH_2 ;

wherein

each X is independently a halogen of atomic number greater than 16 and less than 54 or other leaving group;

each R^{ALK} is independently a linear, branched, or cyclic alkyl (1-20C) group;

each R^{SUB} is independently H, linear, branched, or cyclic alkyl (1-20C), aryl (6-20C), or alkaryl (7-30C);

each R^{ESTER} is independently N-succinimidyl, p-nitrophenyl, pentafluorophenyl, tetrafluorophenyl, pentachlorophenyl, 2,4,5-trichlorophenyl, 2,4-dinitrophenyl, cyanomethyl, 5-chloro,8-quinolone, 1-piperidine, or N-benzotriazole;

each R^B is independently a radical comprising 1-50 atoms selected from the group C, H, N, O, Si, P and S;

each $L^{[2]}$, if present, is independently chosen from the group O, NR^{SUB} and S;

each $J^{[2]}$, if present, is independently chosen from the group C(=O) and C(=S);

each $Z^{[2]}$, if present, is independently a radical comprising 1-200 atoms selected from the group C, H, N, O, Si, P and S, and forming attachment sites for at least $p^{[2]}$ functional groups, wherein the attachment sites are alkyl, alkenyl, or aromatic carbon atoms;

and wherein $Z^{[2]}$, if present, optionally further comprises one or more polyethylene oxide groups;

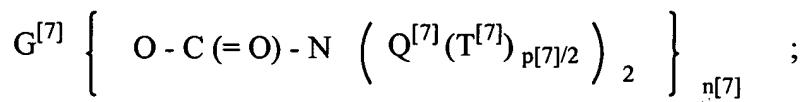
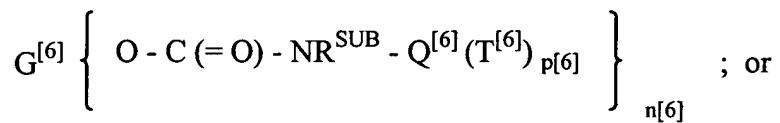
$n^{[1]}$, if present, is 1 to 32;

$n^{[2]}$, if present, is 1 to 32;

$p^{[2]}$, if present, is 1 to 8; with the proviso that the product $n^{[2]} \times p^{[2]}$ be greater than 1 and less than 33;

with the proviso that the valency platform molecule comprises at least 2 polyethylene oxide groups each having a molecular weight of greater than about 5,000 Da, and wherein the total of the molecular weights of all polyethylene oxide groups in the valency platform molecule in combination is greater than about 18,000 Da.

Claim 94 (Currently amended): A ~~conjugate of a chemically defined valency platform molecule and a biologically active molecule, wherein the valency platform molecule prior to conjugation with the biologically active molecule has~~ having the structure of one of the following formulae:



wherein

each of $G^{[6]}$ and $G^{[7]}$, if present, is independently a linear, branched or multiply-branched chain comprising 1-2,000 chain atoms selected from the group C, N, O, Si, P and S;

and wherein $G^{[6]}$ and $G^{[7]}$, if present, optionally further comprises one or more polyethylene oxide groups;

each $T^{[6]}$ and each $T^{[7]}$, if present, is independently chosen from the group NHR^{SUB} , $C(=O)NHNHR^{SUB}$, $NHNHR^{SUB}$, $C(=O)OH$, $C(=O)OR^{ESTER}$, $C(=O)OC(=O)R^B$, $C(=O)X$, $S(=O)_2X$, $C(=NR^{SUB})OR^{SUB}$, NCO , NCS , $OC(=O)X$, $C(=O)OC(=NR^{SUB})NHR^{SUB}$, $C(=O)H$, $C(=O)R^B$, SH , OH , $C(=O)CH_2X$, $R^{ALK}X$, $S(=O)_2OR^{ALK}X$, $N-C(=O)CH=CHC(=O)-NR^1R^2$ wherein R^1R^2 is $-C(=O)CH=CHC(=O)-$, $C(=O)CR^B=CR^B_2$, $R^{ALK}-Hg-X$, $S(=O)CR^B=CR^B_2$, and ONH_2 ;

wherein

each X is independently a halogen of atomic number greater than 16 and less than 54 or other leaving group;

each R^{ALK} is independently a linear, branched, or cyclic alkyl (1-20C) group;

each R^{SUB} is independently H, linear, branched, or cyclic alkyl (1-20C), aryl (1-20C), or alkaryl (1-30C);

each R^{ESTER} is independently N-hydroxysuccinimidyl, p-nitrophenoxy, or pentafluorophenoxy;

each R^B is independently a radical comprising 1-50 atoms selected from the group C, H, N, O, Si, P and S;

n^[6], if present, is 1 to 32;

p^[6], if present, is 1 to 8;

with the proviso that the product n^[6] x p^[6] be greater than 1 and less than 33;

n^[7], if present, is 1 to 32;

p^[7], if present, is 1 to 8;

with the proviso that the product n^[7] x p^[7] be greater than 1 and less than 33;

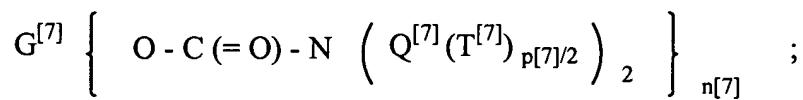
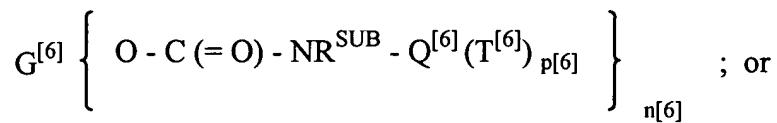
each Q^[6] and each Q^[7], if present, is independently a radical comprising 1-100 atoms selected from the group C, H, N, O, Si, P and S, and wherein each Q^[6] and Q^[7] moiety, if present, forms attachment sites for at least p^[6] or p^{[7]/2} functional groups, respectively, wherein the attachment sites are alkyl, alkenyl, or aromatic carbon atoms;

and wherein $Q^{[6]}$ and $Q^{[7]}$, if present, optionally further comprises one or more polyethylene oxide groups; and

wherein $p^{[7]/2}$ is an integer;

with the proviso that at least one of the $G^{[6]}$, $G^{[7]}$, $Q^{[6]}$, or $Q^{[7]}$ groups comprises a high molecular weight polyethylene oxide group having a molecular weight of at least greater than about 18,000 Da.

Claim 95 (Currently amended): A ~~conjugate of a chemically defined valency platform molecule and a biologically active molecule, wherein the valency platform molecule prior to conjugation with the biologically active molecule has having~~ the structure of one of the following formulae:



wherein

each of $G^{[6]}$ and $G^{[7]}$, if present, is independently a linear, branched or multiply-branched chain comprising 1-2,000 chain atoms selected from the group C, N, O, Si, P and S;

and wherein $G^{[6]}$ and $G^{[7]}$, if present, optionally further comprises one or more polyethylene oxide groups;

each $T^{[6]}$ and each $T^{[7]}$, if present, is independently chosen from the group NHR^{SUB} , $C(=O)NHNHR^{SUB}$, $NHNHR^{SUB}$, $C(=O)OH$, $C(=O)OR^{ESTER}$, $C(=O)OC(=O)R^B$, $C(=O)X$, $S(=O)_2X$, $C(=NR^{SUB})OR^{SUB}$, NCO , NCS , $OC(=O)X$, $C(=O)OC(=NR^{SUB})NHR^{SUB}$, $C(=O)H$, $C(=O)R^B$, SH , OH , $C(=O)CH_2X$, $R^{ALK}X$, $S(=O)_2OR^{ALK}X$, $N-C(=O)CH=CHC(=O)-NR^1R^2$ wherein R^1R^2 is $\underline{-C(=O)CH=CHC(=O)-}$, $C(=O)CR^B=CR^B_2$, $R^{ALK}-Hg-X$, $S(=O)CR^B=CR^B_2$, and ONH_2 ;

wherein

each X is independently a halogen of atomic number greater than 16 and less than 54 or other leaving group;

each R^{ALK} is independently a linear, branched, or cyclic alkyl (1-20C) group;

each R^{SUB} is independently H, linear, branched, or cyclic alkyl (1-20C), aryl (1-20C), or alkaryl (1-30C);

each R^{ESTER} is independently N-hydroxysuccinimidyl, p-nitrophenoxy, or pentafluorophenoxy;

each R^B is independently a radical comprising 1-50 atoms selected from the group C, H, N, O, Si, P and S;

$n^{[6]}$, if present, is 1 to 32;

$p^{[6]}$, if present, is 1 to 8;

with the proviso that the product $n^{[6]} \times p^{[6]}$ be greater than 1 and less than 33;

$n^{[7]}$, if present, is 1 to 32;

$p^{[7]}$, if present, is 1 to 8;

with the proviso that the product $n^{[7]} \times p^{[7]}$ be greater than 1 and less than 33; each $Q^{[6]}$ and each $Q^{[7]}$, if present, is independently a radical comprising 1-100 atoms selected from the group C, H, N, O, Si, P and S, , and wherein each $Q^{[6]}$ and $Q^{[7]}$ moiety, if present, forms attachment sites for at least $p^{[6]}$ or $p^{[7]/2}$ functional groups, respectively, wherein the attachment sites are alkyl, alkenyl, or aromatic carbon atoms;

and wherein $Q^{[6]}$ and $Q^{[7]}$, if present, optionally further comprises one or more polyethylene oxide groups; and

wherein $p^{[7]/2}$ is an integer;

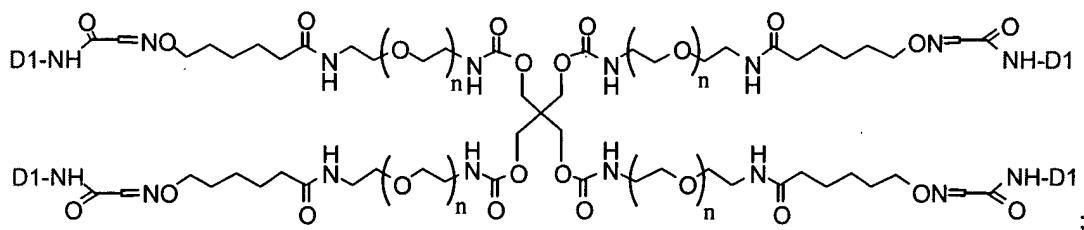
with the proviso that the valency platform molecule comprises at least 2 polyethylene oxide groups each having a molecular weight of greater than about 5,000 Da, and wherein the total of the molecular weights of all polyethylene oxide groups in the valency platform molecule in combination is greater than about 18,000 Da.

Claim 96 (New): A composition comprising conjugates comprising biologically active molecules and the valency platform molecules according to claim 61.

Claim 97 (New): The composition of claim 96, wherein the biologically active molecules are selected from the group consisting of a polysaccharide, a polypeptide, a nucleic acid, and a lipid.

Claim 98 (New): The composition of claim 96, wherein the biologically active molecules are polypeptides.

Claim 99 (New): A conjugate of a valency platform molecule and a biologically active molecule, having the formula:



wherein the molecular weight of the polyethylene oxide groups in combination is 26,400-44,000 Da; and

wherein D1 in said structures is a polypeptide consisting of amino acids No. 2-63 of SEQ ID NO: 2.

Claim 100. (New) A composition comprising conjugates comprising biologically active molecules and the valency platform molecules according to any one of claims 84-95.

Claim 101. (New) A pharmaceutically acceptable composition comprising the composition of claim 100 and a pharmaceutically acceptable carrier.

Claim 102. (New) The composition of claim 20, wherein the biologically active molecules comprise said nucleic acid.

Claim 103. (New) The composition of claim 21, wherein the biologically active molecules are β 2GPI domain 1 polypeptides.

Claim 104 (New) A pharmaceutically acceptable composition comprising the composition of claim 19 and a pharmaceutically acceptable carrier.

Claim 105 (New) A pharmaceutically acceptable composition comprising the composition of claim 20 and a pharmaceutically acceptable carrier.

Claim 106 (New) A pharmaceutically acceptable composition comprising the composition of claim 21 and a pharmaceutically acceptable carrier.

Claim 107 (New) A pharmaceutically acceptable composition comprising the composition of claim 22 and a pharmaceutically acceptable carrier.

Claim 108 (New) A method of making the conjugates according to claim 17 or 96, comprising covalently bonding the biologically active molecules to the valency platform molecules to form conjugates.

Claim 109 (New) A method for treating an antibody mediated disease, comprising administering to the individual an effective amount of the composition according to claim 17 or 96.